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Rare Chromosomal Anomalies Involving Trisomy 12p and 2q37 Deletion in a 10- Month Old Male Child

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Abstract

Trisomy 12p and 2q37 deletions are rare chromosomal anomalies with significant clinical implications, including developmental delays and distinct dysmorphic features. In this case report, a 10-month-old male with trisomy 12p13 and a 2q37 deletion presented with global hypotonia, developmental delays, and dysmorphic features. The patient was born full-term via cesarean section due to cephalopelvic disproportion, with an uneventful antenatal period. Family history was positive for consanguinity. Physical examination showed microcephaly, a broad forehead, bitemporal narrowing, upward slanting eyes, a small mouth, thin lips, and small fingers. Genetic testing confirmed chromosomal abnormalities, leading to a multidisciplinary management approach involving audiology, endocrinology, and surgical consultations, with long-term care focusing on rehabilitation and genetic counseling. Parents were informed about recurrence risk if a balanced translocation is confirmed. This case highlights the importance of early genetic testing in children with unexplained developmental issues and the need for comprehensive, coordinated care to address the multifaceted challenges associated with rare chromosomal anomalies.

Keywords: Trisomy 12p13, 2q37 Deletion, Developmental Delays, Chromosomal Anomalies, Genetic Counseling.

Introduction

Trisomy of the short arm of chromosome 12 (12p) is an exceptionally rare chromosomal anomaly, with an estimated incidence of approximately 1 in 50,000 live births.[1] The first case of trisomy 12p was reported by Uchida and Lin in 1973, attributed to the malsegregation of a balanced parental chromosome rearrangement[2]. This duplication typically occurs either spontaneously (de novo) or because of malsegregation from a balanced translocation inherited from a parent[1].Duplication 12p may also arise de novo from misalignment of low copy repeats (LCRs) through non-allelic homologous recombination (NAHR)[3].

Clinically, duplication of chromosome 12p is associated with several phenotypic features, including increased birth weight, hypotonia, craniofacial anomalies (such as turricephaly, macrocephaly, frontal bossing, a wide nasal bridge, a short nose, a thin upper lip, and dysmorphic ears), intellectual impairment, and moderate psychomotor delay[4,5].

Deletions in the distal 2q37 region affect the final cytogenetic band on the long arm of chromosome 2, which is categorized into three sub-bands: 2q37.1, 2q37.2, and 2q37.3. The 2q37.3 sub-band includes a small subtelomeric area, known as 2qtel, where non-harmful polymorphic deletions or duplications can occur. Detailed mapping of deleted regions is uncommon, as most cases are identified using conventional cytogenetics, subtelomeric FISH, or microsatellite markers, with array-CGH being used only in a few studies[6]. Deletions in the distal 2q37 region are characterized by a distinct set of clinical manifestations, including mild to moderate developmental delay, intellectual disability, brachydactyly of the 3rd to 5th digits or toes, short stature, obesity, hypotonia, and a characteristic facial appearance. This region's deletions are also associated with autism spectrum disorder (ASD) and distinctive facial dysmorphisms, such as a prominent forehead, sparse and arched eyebrows, midface hypoplasia, a depressed nasal bridge, a thin upper lip, and various pinna abnormalities, ranging from fleshy or anteverted lobules to microtia[7].

These chromosomal abnormalities, including trisomy 12p and 2q37 deletions, present with a constellation of physical, cognitive, and behavioral characteristics that are crucial for understanding the patient's clinical presentation and guiding management strategies.

Case Presentation

Patient Presentation

A 10-month-old male child presented to LG Hospital with a primary complaint of inability to hold his head. On physical examination, the patient exhibited central global hypotonia, delayed developmental milestones, obesity and distinct dysmorphic features, including microcephaly, a broad forehead, bitemporal narrowing, upward slanting eyes, a small mouth, thin lips, and small fingers. These clinical findings raised the suspicion of an underlying genetic disorder, prompting a comprehensive evaluation of his genetic background.

Figure 1:

Figure 2:

Figure 3:

Antenatal and Birth History

The pregnancy was full-term and ended in a caesarean section due to cephalopelvic disproportion. The antenatal period was uneventful. The patient was admitted to the neonatal intensive unit for large for gestational age (LGA) as the patients birth weight was 4.2 kilograms.

Family History

The patient's family history is significant for second degree consanguineous marriage which increases the likelihood of autosomal recessive genetic disorders.

Clinical Examination

At the time of examination, the child weighed 10.7 kg. Auditory evaluation using Distortion Product Otoacoustic Emissions (DPOAE) testing indicated mild hearing loss in the right ear and minimal hearing loss in the left ear. A neurological evaluation, including MRI of the brain, did not reveal any abnormalities. 2D Echocardiography was also done and it was suggestive of Patent Foramen Ovale (PFO) with left to right shunt.

Laboratory and Genetic Investigations

Laboratory tests, including serum thyroid-stimulating hormone (TSH) and serum homocysteine levels, were within normal ranges. However, genetic testing through whole exome sequencing revealed significant findings, including a pathogenic chromosome 12 duplication (3 copies) in the 12p13 region and a pathogenic chromosome 2 deletion (1 copy) in the 2q37 region. These chromosomal abnormalities are associated with developmental delays, growth issues, and various congenital anomalies. Genetic consultation highlighted the possibility of a balanced translocation in one of the parents, potentially responsible for the observed chromosomal abnormalities in the child.

Figure 4:

Genetic analysis report showing duplication of Chromosome 12 and deletion of Chromosome 2.

Management Plan

Neuro-rehabilitation: Multidisciplinary approach was required for this patient such as Occupational Therapy, Speech Therapy, and Physical Therapy to address motor skill deficits and developmental delays.

Nutrition: Dietary management is crucial to address potential obesity, a risk associated with the identified chromosomal abnormalities. Also the patient was advised to start multivitamin supplements in view of other dietary challenges.

Genetic Counseling: The parents were advised to consider couple karyotyping to assess the possibility of a balanced translocation, which could inform the risk of recurrence in future pregnancies.

Parental Guidance and Follow-Up: Ongoing parental guidance includes the continuous monitoring of the child's growth, developmental progress, and nutritional status. The child requires close follow-up across multiple specialties, including cardiology, audiology, endocrinology, and genetics. Comprehensive counseling was provided to the parents to ensure they understand the genetic findings, the need for ongoing care, and the implications for future pregnancies.

Discussion

This case report discusses a rare occurrence of chromosomal anomalies involving trisomy of the 12p13 region and a deletion in the 2q37 region in a 10-month-old male patient. These chromosomal abnormalities, uncovered through whole exome sequencing, highlight the complex and varied genetic factors that contribute to developmental delays, growth problems, and congenital anomalies.

Trisomy 12p13

Trisomy 12p is an uncommon chromosomal anomaly characterized by the duplication of a segment of the short arm of chromosome 12. The 12p13 region houses several essential genes that play a critical role in normal development. An extra copy of this region can lead to a broad range of clinical symptoms. These can include growth retardation, developmental delays, intellectual disabilities, and distinct craniofacial features[8].

The clinical impact of trisomy 12p varies greatly, depending on the size of the duplicated segment and other genetic factors[9].

In this case, the identified duplication likely contributes to the patient's developmental and growth challenges. However, due to the variability in clinical presentation, further investigation into the specific genes within the duplicated region is necessary to fully understand the impact of this trisomy.

2q37 Deletion

A deletion in the 2q37 region represents another rare chromosomal disorder that is linked to a variety of developmental and physical anomalies. The 2q37 region contains genes that are crucial for skeletal development, cognition, and metabolic regulation. A deletion in this area generally leads to a characteristic set of symptoms, including intellectual disability, short stature, brachydactyly, and sometimes autism spectrum disorder. The clinical variability seen in 2q37 deletion syndrome is due to the size of the deleted region and the specific genes involved[6]. In this patient, the 2q37 deletion likely plays a significant role in the observed developmental delays and other clinical features, highlighting the importance of detailed genetic testing in diagnosing and managing such cases.

Parental Genetic Considerations

The potential for a balanced translocation in one of the parents, as indicated by genetic consultation, raises critical considerations regarding the recurrence risk in future pregnancies. Carriers of balanced translocations typically do not exhibit abnormal phenotypes because there is no net gain or loss of genetic material. However, during gametogenesis, an unbalanced translocation can occur, resulting in offspring with duplications or deletions, as seen in this case. Thus the substantial risk of recurrence underscores the importance of thorough genetic counseling and the consideration of options such as prenatal diagnosis or preimplantation genetic testing in future pregnancies[10].

The co-occurrence of trisomy 12p13 and 2q37 deletion in this patient presents a unique clinical challenge, given the overlapping and potentially interacting effects of these chromosomal abnormalities[11]. This case emphasizes the importance of comprehensive genetic testing in children with unexplained developmental delays and congenital anomalies. The findings also stress the necessity for ongoing monitoring and multidisciplinary management to address the wide-ranging medical, developmental, and psychosocial needs of affected individuals.

The patient exhibited developmental delays, dysmorphic features, mild hearing loss, leading to a suspected genetic disorder and further genetic testing [12].

The patient's family history is significant for consanguinity, as his parents are first cousins, which increases the likelihood of autosomal recessive genetic disorders[13].

Conclusion

This case study details a 10-month-old boy with rare chromosomal abnormalities, specifically a trisomy of 12p13 and a deletion in 2q37. These genetic anomalies contribute to a complex clinical picture, characterized by dysmorphic features, and developmental delays. Comprehensive genetic evaluation and targeted management strategies were implemented to address the immediate and long-term needs of the patient. The findings underscore the importance of early genetic testing and multidisciplinary care in managing rare genetic disorders. Genetic counseling for the parents emphasized the significant risk of recurrence in future pregnancies, highlighting the necessity for ongoing monitoring and informed decision-making.

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